Remarks

Applicant reviewed the Office Action dated February 19, 2003, and the documents cited therewith. In response to the Office Action dated February 19, 2003, reconsideration and withdrawal of the rejection, in view of the remarks and amendments presented herein, is respectfully requested. Claims 8, 10-11, and 23-24 have been amended, claims 26 and 28 have been cancelled without prejudice or disclaimer; as a result, claims 8, 10-12, 23-25, 27 and 29-30 are pending in the instant application.

Claims 8 and 24 have been amended for the sake of improved clarity, and not for any reason relating to the patentability of these claims. Claim 10 has been amended to be dependent on claim 8 instead of claim 23. Claims 11 and 23 have been amended for consistency with amended claim 8.

Rejection under 35 U.S.C. § 103(a)

Claims 8, 10-12 and 23-30 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Davis in view of Sagusa, Gimpel, Simon and Christenson, Leissing or Mullins. Applicant respectfully traverses the rejection.

Davis discloses a method of estimating a change in an analyte in a whole-blood sample, which is due to the hemolysis of red blood cells, comprising separating a plasma fraction from the whole blood sample, estimating the quantity of extracellular hemoglobin in the plasma fraction, estimating a change in the analyte concentration in the sample due to the hemolysis of whole blood cells, and adjusting the apparent concentration of the analyte to account for the proportion of same which is due to the hemolysis of red blood cells (column 6, lines 3-16; column 8, lines 40-56).

Davis discloses that the amount of hemoglobin in the plasma sample may be determined by measuring the reflectance of the sample using a wavelength at which hemoglobin exhibits a maximum absorbance, and by using a graph of reflectance vs. hemoglobin concentration, derived from a set of samples containing known amounts of hemoglobin, to determine the concentration of hemoglobin in the plasma sample (column 8, lines 18-21 and 28-36). Davis, however, does not teach or suggest a method for determining the concentration of one, or more than one analyte in a specimen comprising a blood substitute interferent, as recited in claim 8. In particular,

Davis does not disclose or suggest a method comprising a step of providing a calibration algorithm for a blood substitute interferent, and which involves determining a corrected concentration of one, or more than one analyte using the calibration algorithm. Furthermore, Davis does not disclose or suggest a method as recited in claim 24, which comprises using separate calibration algorithms to determine the presence of pseudohemolysis and hemolysis in a specimen.

Christenson et al. disclose that hemoglobin based blood substitutes interfere with routine chemical tests, and the dilution of the sample is suggested as a way to avoid interference. There is no teaching or suggestion in Christenson et al. as to how an interferent may be identified and/or quantified in a blood sample comprising a blood substitute. Applicant, therefore, submits that Christenson et al. help define the problem in the art that the present invention is solving, that being, determining the concentration of an interferent in a sample, and if desired, correcting for the concentration of the interferent when establishing the concentration of an analyte in the sample.

Leissing et al. disclose modifications of clinical chemistry methods to overcome interferences from diaspirin crosslinked haemoglobin (DCLHb). The abstract teaches that filtering samples through an Amicon Centrifree micropartition system can remove concentrations of DCLHb up to 5000 mg/dl, producing a filtrate with molecular weight constituents less than 30000 daltons. Furthermore, for the detection of some analytes, dilution of the sample is required, in a method similar to that disclosed in Christenson et al. Leissing et al. do not teach or suggest the subject matter that is recited in the claims of the instant application. Leissing et al., as noted for Christenson et al., define the problem in the art that is solved by the claimed invention.

Mullins et al. disclose that fluosol may lead to potential errors in the analysis of blood specimens. There is no disclosure or suggestion as to how an interferent may be identified and/or quantified in a blood sample that comprises a blood substitute. Rather, Mullins et al. further define the problem that is solved by the claimed invention is addressed to solving.

The Examiner has alleged that it would have been obvious to one of ordinary skill in the art at the time the invention was made to include substances such as blood substitutes disclosed by Christenson et al., Leissing et al., or Mullins et al. as interfering substances into the correction method of Davis. Applicant respectfully disagrees. Davis in combination with Christenson et

al., Leissing et al., or Mullins et al. do not disclose or suggest all the elements of any of the pending claims. None of the cited documents disclose or suggest a method for determining the concentration of one, or more than one analyte in a specimen comprising a blood substitute interferent, as recited in claim 8. None of the documents disclose or suggest a method comprising a step of providing a calibration algorithm for a blood substitute interferent, and which involves determining a corrected concentration of one, or more than one analyte using the calibration algorithm. Additionally, none of the documents disclose or suggest a method as recited in claim 24, which comprises using separate calibration algorithms to determine the presence of pseudohemolysis and hemolysis in a specimen. Thus, whether taken alone or combined, the documents do not disclose or suggest all the elements of any of the instant claims.

Furthermore, the combination of the cited documents provides no suggestion or motivation to modify the disclosure of Davis to arrive at the invention of claims 8, 10-12, 23-25, 27 and 29-30. The cited documents also provide no reasonable expectation of success at practicing a method for determining a corrected concentration of one, or more than one analyte in a specimen comprising a blood substitute interferent, where the method involves measuring an absorbance or reflectance of radiation of the specimen, wherein the measuring step is performed in the absence of any reaction step that generates a chromophore within the specimen or a method for determining the presence of true hemolysis or pseudo-hemolysis in a sample. Thus, the cited documents fail to provide any of the three requirements for a *prima facie* case of obviousness over claims 8, 10-12, 23-25, 27 and 29-30.

The Examiner has also alleged that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use different wavelengths as taught in Sagusa to differentiate between true hemolysis and plasma discoloration due to circulating colored substances as taught by Simon et al. in the Davis method. Applicant respectfully disagrees.

The Sagusa patent discloses a colorimetric method for measuring components in a sample in the presence of interfering chromogens. In the method disclosed in the Sagusa patent, a color former is added to blood samples for coloring, and measurements for specific components are determined based on the light absorbance caused by the coloring. The measurements for specific components are corrected by the degree of chyle, degree of hemolysis and degree of icterus, which are determined at different wavelengths.

Simon et al. disclose that iron dextran therapy may cause a red-brown discoloration of the plasma simulating a hemolytic transfusion reaction. The method used in Simon et al. to detect the iron, comprises adding Gomori's iron stain (page 342, last paragraph, left hand column) and obtaining a blue color.

There is no disclosure or suggestion in Sagusa or Simon et al. of a method of determining the concentration of an analyte in a specimen using the method as defined in claim 8 or 24 of the present application, as no exogenous reagent is added to the sample in the methods defined in the claims of the present application. It is, therefore, respectfully asserted that even if the calibration algorithms of claims 8 and 24 are construed as being algorithms developed using analyses of absorbance or reflectance over a plurality of wavelengths, the methods defined by the present claims do not involve a step of converting an analyte to a chromophore, as required by the method of Sagusa or Simon et al. One skilled in the art would not, therefore, be motivated to combine the disclosures of Sagusa and Simon et al. with that of Davis, and one, or more of Christenson et al., Leissing et al. or Mullins et al. to arrive at the presently claimed invention.

The Examiner has further alleged that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a derivative spectroscopic method as shown by Gimpel for correction in the Davis method. Applicant respectfully disagrees.

Gimpel et al. disclose a method of measuring total bilirubin concentrations in cerebrospinal fluid by using derivative spectroscopy and the formation of azobilirubin derivatives. Gimpel et al. do not, however, provide any disclosure or suggestion of a method for determining the concentration of bilirubin without using azobilirubin derivatives.

It is respectfully asserted that even if the calibration algorithms of claims 8 and 24 are construed as being algorithms developed using derivative analyses of spectra, the methods defined by the present claims do not involve a step of converting an analyte to a chromophore, as required by the method of Gimpel et al. One skilled in the art would not, therefore, be motivated to combine the disclosure of Gimpel et al. with that of Davis, and one or more of Christenson et al., Leissing et al. or Mullins et al. to arrive at the presently claimed invention.

Applicant, therefore submits that Davis, in combination with of Christenson et al., Leissing et al. or Mullins et al., and any of the other cited documents does not teach or suggest the method of determining the concentration of an analyte in a specimen containing a blood substitute interferent, as claimed in claims 8 , 10-12, 23 and 25-30. Furthermore, Applicant

respectfully submits that Davis in combination with Christenson et al., Leissing et al. or Mullins et al., or any of the other cited documents, does not teach or suggest the method of determining the presence of true hemolysis or pseudo-hemolysis in a specimen, as claimed in claim 24. Thus, Applicant respectfully requests withdrawal of the rejection of the claims under 35 U.S.C. § 103(a).

Conclusion

Claims 8, 10-11, and 23-24 have been amended, claims 26 and 28 have been cancelled without prejudice or disclaimer; as a result, claims 8, 10-12, 23-25, 27 and 29-30 are pending in the instant application.

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's representative (612 373-6905) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, Washington, D.C. 20231, on this 19th day of May, 2003.

Patricia A. Hulke
Name

Signature.